UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/873,403	06/04/2001	Pramod K. Srivastava	8449-178-999	1802

20583 7590 11/17/2004

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/873,403	SRIVASTAVA, PRAMOD K.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-9,40 and 42-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-9,40 and 42-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/5/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Re: Srivastava *et al*
Priority Date: 02 June 2000

1. The amendment filed 8/26/2004 is acknowledged and entered into the record. Accordingly, claims 2-6, 10-39, and 41 are canceled without prejudice or disclaimer, and claim 50 is newly added.

2. Claims 1,7-9,40, and 42-50 are pending and examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The declaration filed 4/5/2004 by Dr. Srivastava (herein Srivastava Declaration) is acknowledged and considered.

Information Disclosure Statement

5. The Information Disclosure Statement filed 4/5/2004 is acknowledged and considered. A signed copy of the IDS is attached hereto.

Claim Rejections Maintained - 35 USC § 112, 1st paragraph

6. The rejection of claims 1,7-9,40, 42-49 and now newly added claim 50 under 35 USC § 112,1st as lacking an enabling disclosure is maintained for the reasons of record. Applicant argues that one of skill in the art would be capable of using the instant invention without undue experimentation because the specification provides sufficient guidance on how to prevent diseases such as cancer or HIV (see page 11 of the response filed 4/5/2004). To support the assertion of lack of undue experimentation,

the applicant relies on the Srivastava Declaration. More specifically, applicant states that the declaration teaches the "prevention and /or delaying" of cancer (see page 11 of the response). The Srivastava Declaration teaches that upon administration of the α 2 Macroglobulin-OVA20 complex to mice inoculated with tumors, that there was a inhibitory effect due to the complexed molecule (see points 8-9 of the declaration). Applicant concludes that this is sufficient evidence to support the claims drawn to prevention of cancer and HIV. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. Reasonable guidance with respect to what is being claimed and that which is taught in the specification is required for there to be an enabling disclosure. However, one cannot extrapolate the teachings of the specification to the scope of the claims because the specification provides no exemplification of or guidance on how to use the claimed α 2 macroglobulin complex for immunization or prevention purposes with any predictability.

Applicant's reliance on the Srivastava Declaration does not overcome the lack of guidance in the specification regarding the prevention of cancer and especially not for HIV. As stated previously, reasonable guidance with respect to preventing cancer relies on quantitative analysis from defined populations which have been successfully pre-screened and are predisposed to particular types of cancer. This type of data might be derived from widespread genetic analysis, cancer clusters, or family histories. The essential element towards the validation of a preventive therapeutic is the ability to test the drug on subjects monitored in advance of clinical cancer and *link* those results with subsequent histological confirmation of the presence or absence of disease. This

irrefutable link between antecedent drug and subsequent knowledge of the prevention of the disease is the essence of a valid preventive agent. Further, a preventive administration also must assume that the therapeutic will be safe and tolerable for anyone susceptible to the disease. In the instant case (such as the one provided in the Srivastava Declaration), the mice were subject to inoculation and subsequently challenged with a tumor of known origin. This type of challenge is not indicative of the normal occurrences of cancer, because it can not be predicted what type of cancer will develop and one of skill in the art cannot predict with any certainty that amongst the population there will be those who require such preventive treatment. Moreover, the skilled artisan cannot determine which type of antigenic determinant should be administered to specific individuals without knowing what type of cancer those individuals will require. It cannot be readily predicted whether an individual will develop a specific type of cancer, take for example a carcinoma. How would one of skill in the art know how to administer an α 2M-carcinoma specific antigenic determinant complex and be assured that that complex would be effective at "preventing" that carcinoma? Furthermore, the use of experimental animal models is not predictive or correlative to human subjects. For example, Byers, T. (CA Journal, Vol. 49, No. 6, Nov/Dec. 1999) teaches that randomized controlled trials are commonly regarded as the definitive study for proving causality (1St col., p.358), and that in controlled trials the random assignment of subjects to the intervention eliminates the problems of dietary recalls and controls the effects of both known and unknown confounding factors. Further, Byers suggests that chemo-preventative trials be designed "long-term" such that testing

occurs over many years (2 col., p. 359). Thus while the declaration provides enablement for the prevention of tumors in a mice, in no way does this extrapolate to any therapeutic efficacy to the human population. Such guidance has not been provided in the specification or in the Srivastava Declaration.

In addition, applicant has not provided any indication or evidence that refutes the arguments concerning the prevention of infectious diseases caused by HIV. Therefore, in view of the fact that the specification teaches the general disclosure of desired embodiments of α 2 macroglobulin-antigen complexes, that the specification does not provide specific working examples with regard to the use of the claimed complexes for in prevention of diseases as claimed, the rejection of claims under 35 USC 112, 1st paragraph is maintained for the reasons of record.

Claim Rejections Maintained - 35 USC § 112, 1st paragraph

7. The rejection of claims 1,7-9,40,42-49 and now newly added claim 50 under 35 USC § 112, 1st paragraph as lacking written description is maintained for the reasons of record. Applicant argues the written description for the "antigenic molecule displaying the antigenicity of an antigen over expressed in a cancer cell relative to its expression in a noncancerous cell of the said cell type" is sufficiently disclosed in the specification so as to convey to one of skill in the art that the applicant was in possession of the claimed subject material. More specifically, applicant argues that given the high level of skill in the art the specification need not teach all embodiments of to exacting detail. Applicant substantiates their arguments by stating that if the specification provides sufficient

physical, chemical or functional characteristics, written description is improper (see page 15-16). Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record.

An application may show written description if the specification discloses sufficient detail or relevant identifying characteristics which provide evidence that the applicant was in possession of the claimed invention, such as through complete and partial structure, or other physical or chemical properties or functional characteristics coupled with a known or disclosed correlation between function and structure. In the instant case, the specification has only taught tumor antigens or infectious agents (see page 37, lines 13-36, for example), and has not taught antigenic molecules that display the antigenicity of an antigen over expressed in a cancer cell relative to its expression in a noncancerous cell" nor an "antigenic molecule of an infectious agent". Neither the claims nor the specification teach any identifiable characteristics that are associated with these "antigenic molecules which displays the antigenicity" of a tumor or infectious agent. Furthermore, the specification does not provide sufficient representative species to enable the full scope of the genus claimed. Although the tumor associated antigens (see page 37) and the infectious agents (see page 37) are known to those skilled in the art and need not be described in detail, the determinants of "antigenicity" have not been sufficiently disclosed in the specification, and such is not conventionally taught or known in a highly unpredictable art, such as peptide chemistry or antigenic epitope determination. Furthermore, although the determination of such epitopes may be routine in the art, the general knowledge and level of skill in the art does not supplement

the omitted disclosure because specific, not general, guidance is what is needed. Thus given the highly variant nature of antigenic molecules and determinants of "antigenicity", the lack of proper representative species to establish broad coverage of the genus of "antigenic molecules which displays the antigenicity" of tumor antigens or infectious agents, and the lack of identifiable characteristics, the rejection of 35 USC 112, 1st paragraph as lacking written description is maintained.

New Arguments

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 1,7-9,40,42-50 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility. The fact pattern for this case is similar to those established in the Utility Guidelines (example 2) – published at http://www.uspto.gov/web/offices/pac/utility/utilityguide.pdf .

The broadest reasonable interpretation of the claims in this situation is prevention of cancer or the prevention of diseases associated with HIV. In this rejection it is presumed that applicants intend to prevent cancer or diseases associated with HIV. The prevention of cancer or the prevention of diseases associated with HIV is itself not credible on its face in view of the contemporary knowledge in the art. No compound is

currently available or known to prevent cancer or diseases associated with HIV, such as AIDS, which would have these effects.

In general, the treatment of cancer is at most unpredictable as underscored by Gura (Science, v278, 1997, pp.1041-1042, previously cited) who discusses the potential shortcomings of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with clonogenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041, 1st column) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive. Therefore, given the unpredictable nature with regard to treating cancer, it would not be credible on its face that a composition would be capable of preventing cancer.

Furthermore, with regard to the prevention of diseases associated with HIV, there are no options for prophylactic treatment. Beyrer C (The Hopkins HIV Report 2003 Jan; 15(1):6-7, previously cited) underscores the importance of establishing a vaccine for preventing HIV, but clearly states that although the parameters for understanding the progression of the disease exist, methods or treatment options are lacking.

Thus given the current state of the art with regard to preventing cancer or diseases associated with HIV, such as AIDS, the utility for a pharmaceutical compound is not on its face a credible utility.

10. Claims 1,7-9,40, and 42-50 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

All other rejections are withdrawn in view of the applicant's amendments and arguments thereto as set forth in a paper filed 4/5/2004 and 8/26/2004.

Conclusion

11. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art Unit 1642
November 3, 2004

GARY NICKOL
PRIMARY EXAMINER